Vaccine hesitation and the ‘pandemic’ of the unvaccined: What to do to face the new “Vaccine Revolt”?

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ABSTRACT
The frequency of people hesitating to get vaccinated is increasing worldwide and regarding the covid-19 pandemic, this phenomenon has been increasingly noticed at a national level. This article exposes a brief presentation of the historical factors of this phenomenon, approaches its main determinants and conceptual model, in addition to presenting a set of communication strategies in vaccine health that can be implemented to face this problem to raise the credibility and adherence to immunizations.

Keywords: Vaccines, Vaccination coverage, Vaccination refusal, anti-vaccination movement, Covid-19.
INITIAL CONSIDERATIONS

"Except for drinking water, no other modality, not even antibiotics, has had as much effect in reducing mortality and in population growth as vaccines".

The discovery of the first safe method of vaccination is attributed to the British physician Edward Jenner. The researcher after 20 years of study showed that protection against smallpox disease could be obtained with the inoculation of material extracted from a human pustular lesion resulting from a case of cowpox. Jenner extracted the active secretion from a wound ("pus") present on the hand of a cow milker who had contracted smallpox from her animals and inoculated it into a healthy boy, James Phipps, age eight, on May 4, 1796. The boy mildly contracted the disease and then was cured. After the successful experiment, Jenner named the material vaccine, derived from the Latin term vacca, and the process named vaccination. Only after almost a century in 1885, Louis Pasteur, a French chemist, developed a new product against human rabies and, in honor of Jenner, called this material a "vaccine". This was the first rabies vaccine in human history.

From this moment onward, with the promising results that were shown, new researches started to be developed around the world and culminated in the development of one of the most important measures in the prevention of preventable infectious diseases that are known to this day - the immunizations.

In the current era, vaccines are undoubtedly considered one of the greatest achievements of man on Earth – just look at the effect of vaccination on the curve of those infected by Covid-19 and how much the advancement of immunization has brought benefits to nations. These technologies are classified as one of the most successful technologies ever developed in the context of Preventive Medicine to protect human health, second only to basic sanitation actions, in particular the supply of drinking water.

It is estimated that more than 4 million deaths are prevented each year through vaccination worldwide. In the Bulletin of the World Health Organization (WHO) it was projected that the mass vaccination of the population currently prevents at least four deaths per minute and generates savings of around 45 million dollars daily across the globe, equivalent to 250 million reais.

Nationally, the offer of vaccines through the National Immunization Program (NIP), created in 1973 was decisive for the successful control of vaccine-preventable diseases in Brazil, including more recently the Covid-19.

The NIP has been bringing relevant results and has greatly contributed to important improvements in the health of the Brazilian population, such as the eradication of smallpox; the elimination of polio and urban yellow fever, the circulation of the measles virus (2016) and rubella (2015); as well as to reduce the incidence of diphtheria, pertussis, meningitis caused by H. influenzae type B, tetanus, tuberculosis in children under 15 years of age, and, more recently, meningitis and pneumonia and the decrease in the overall average of deaths and hospitalizations per million during the covid-19 pandemic.

In this work, we present a brief presentation of the historical factors of vaccine refusal (currently called 'vaccination hesitation'), we approach its main determinants and conceptual model, in addition to presenting a set of health communication strategies that can be implemented with the perspective to enhance credibility and adherence to immunizations.

VACCINE HESITATION AND THE PANDEMY OF THE NON-VACCINED: CONCEPTS, DETERMINANTS AND ACTION STRATEGIES

Despite the facts cited above, many individuals seem hesitant about immunizations, doubting their benefits, worrying about their safety and/or questioning whether they need it or not.

Currently, in general, activists from these anti-vaccine groups use communities on social media such as Facebook and WhatsApp to discuss their fears about immunizations and supposed health risks. The “actions” of this group range from the spread of false side effects from injections to the spreading of misconceptions about the safety and efficacy of doses of immunizers. Such groups question without evidence possible benefits to the pharmaceutical industry, false harm to which children are exposed to when administering combined vaccines, among other inauthentic fears.
Aps et al. highlight that these movements use strategies such as distortion and dissemination of false information, claiming to have a scientific basis, to question the efficacy and safety of vaccines. The researchers bring up that the actions produced by the "anti-vaccination" groups relate to other vaccines, such as the triple viral (measles, mumps and rubella) - MMR, adjuvants present in its composition and the thimerosal preservative with the occurrence of autism and other diseases in children, and they substantiate into temporal associations that bear no basis or causal relationship to vaccines.

The extreme expression of vaccine hesitation, or "vaccination refusal", is a behavior that is not exclusive to modernity and in the national territory dates back to the beginning of the implementation of these technologies as a public health strategy, when for example a popular riot started in mid-November 1904, in the city of Rio de Janeiro, when it was started the historic episode of "Vaccine Rebellion" – a movement in against mandatory smallpox vaccination, whose members considered the legal imposition of smallpox vaccine as a true subversion of freedom over the organism itself. In Figure 1, we present a cartoon published on October 29, 1904, which presents visual information about this event.


1 This was an event between November 12 and 15, in Rio de Janeiro, then capital of Brazil, when the population faced off against Oswaldo Cruz and his health guard. The movement became known as the "Vaccine Revolt" or "Quebra-Lampões" and was carried out in protest against the mandatory requirement of vaccination against smallpox. The action took place in a context of important sanitation and urban reform measures in the government of President Rodrigues Alves (1902-1906) and the Mayor of Rio de Janeiro, Pereira Passos (1902-1906). At its end, on November 16, 1904, the text of the Mandatory Vaccine Law was amended by the National Congress, making smallpox vaccination optional for the population. A few years later, smallpox was eradicated from Brazil.
At an international level, an equally striking episode of persistent mistrust and widespread misconceptions about vaccines began in 1998 when the British journal “The Lancet” published a research by Andrew Wakefield MD, that linked alleged cases of autism with the measles vaccine. Despite the abundance of scientific evidence already produced against the false revelations raised by physician Wakefield and the retraction of his work in 2010 by the Magazine itself, the harmful consequences of that article continue to support groups against vaccination and encourage disbelief about immunizations in the world, events that run against the advances already achieved and brings serious consequences for the health sectors16-18.

The growth of groups against the immunization process, intensified in recent decades by the dissemination of fake news through cyberspace has gained increasingly strength and visibility in the world8-9.

The “anti-vaccination movement” - with its variants, interfaces and consequences - the main factor pointed out by health agencies as a driver of the drop in the number of individuals immunized in vaccination campaigns and the low adherence of the population to vaccination programs on the planet19,21. This “movement” has gained such proportions that it has even been considered by the WHO as one of the ten threats to global health to be faced by nations22. This fact is justifiable and deserves special attention from the health authorities because with the increase in the percentage of sub-immunized individuals, the chances of the resurgence of some diseases eradicated or controlled can also increase.

In Brazil, for example, a study published in 2020 evaluated the trend of vaccination coverage in the country and observed a predisposition to a reduction in the number of immunizations, with drops of 0.9%, 1.3% and 2.7% per year in vaccine coverage for BCG, polio and MMR, in that order23. In the country, the National NIP Surveillance System registers a worrying decrease in vaccination coverage in the last five years and decreases of 10 to 20 percentage points in vaccination coverage in early childhood in recent years24. As a result, outbreaks and epidemics of diseases that were no longer part of the reality of health systems such as Measles, are experiencing a true re-emergence process in various regions of the globe - including Brazil25.

Other recent surveys, including at a national level, already point to resistance, crisis of confidence and (mis)information in the individual-society relationship in the context of the covid-19 pandemic and emphasize that hesitation to vaccines in the current context of covid-19 has gained wide highlight, in part due to the great expressiveness of the online anti-vaccine movement in the era of covid-19 and infodemic26,27.

Concerned with the advancement of this phenomenon globally and in particular with the consequences that this non-adherence to vaccines can bring to society, the WHO created, in 2012, an advisory group in the area of vaccines and immunizations, the Strategic Advisory Group of Experts Working Group on Vaccine Hesitancy (SAGE-WG). This committee was created to define vaccine hesitation, understand its magnitude, identify determining factors, and gather evidence, efforts, policies, and successful strategies in dealing with vaccine hesitation at the global level28.

The SAGE-WG, as one of its first actions dealt with conceptualizing this problem, defining that “vaccination hesitation refers to the delay in accepting or refusing vaccines, despite their availability in vaccination services”. It further established that this phenomenon is complex, varying over time, territory and according to different vaccines and that it is also influenced by factors such as complacency, convenience and confidence - a conceptual model that became known as “3Cs” (Figure two). This milestone appears in order to facilitate the identification of vaccine hesitation in different places on the planet and, thus, better guide the recognition of this behavior and, consequently, the formulation of communication, prevention and health education strategies in this area28,29.

The SAGE-WG specialists also mapped out the main conditions of the phenomenon and established a matrix of determinants of vaccine hesitation. This theoretical model contemplates a set of contextual, individual, group and specific influences of the vaccine(s) and/or the vaccination process that are capable of influencing the decision-making of individuals and/or their guardians to accept, delaying or refusing some or all vaccines from a recommended immunization schedule. These determinants were grouped by SAGE-WG members into three classes: contextual determinants; individual and group determinants; specific issues of the vaccine(s) and the vaccination process.
Contextual determinants include those influences arising from historical, sociocultural, environmental, institutional, health system, economic or political factors; in individual and group determinants, those influences arising from the personal perception of the vaccine or which arise from the social environment or groups to which the individual belongs; and, finally, specific issues of the vaccine(s) and the vaccination process, which involve aspects directly related to the vaccine(s) or the vaccination process. Such factors are summarized in Table 1.

But after all, what to do to face vaccine hesitation and the ‘pandemic’ of the unvaccinated?

In 2019, a systematic review of the literature was carried out to determine effective strategies that could be implemented to encourage families in the United States of America to vaccinate their children. Among the strategies identified by the group of researchers, three main fronts of intervention were present: technological, mass marketing and direct communication actions in health. In the first category, social media platforms, health information technologies and web pages were included as modalities to promote greater vaccine coverage.

Table 1. Determinants of Vaccine Hesitation established by the SAGE-WG.

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<tr>
<th>CONTEXTUAL DETERMINANTS</th>
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<tbody>
<tr>
<td>a. Media</td>
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<td>b. Influential leaders, immunization program managers</td>
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<td>c. Anti- or pro-vaccination pressures</td>
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<tr>
<td>d. historical influences</td>
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<td>e. Religion, Culture, Gender and Socioeconomic Factors</td>
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<td>f. Policy/policies</td>
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<td>g. geographic barriers</td>
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<td>h. Perception of the pharmaceutical industry</td>
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<th>INDIVIDUAL AND GROUP DETERMINANTS</th>
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<tr>
<td>a. Personal, family and/or community member experience with vaccination</td>
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<td>b. Beliefs, attitudes about health and disease prevention</td>
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<tr>
<td>c. Knowledge and confidence in the health system and confidence of professionals</td>
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<tr>
<td>d. Risk/benefit (perceived, speculated)</td>
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<tr>
<td>e. Immunization as a social norm versus not necessary/harmful</td>
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<th>SPECIFIC VACCINE(S) AND VACCINATION ISSUES</th>
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<tr>
<td>a. Risk/benefit (epidemiological and scientific evidence)</td>
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<tr>
<td>b. Introduction of new vaccine or new vaccine formulation or recommendation</td>
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<tr>
<td>c. administration mode</td>
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<tr>
<td>d. Structuring the vaccination program</td>
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<tr>
<td>e. Vaccination strategy (regular calendar or campaign)</td>
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<td>f. Reliability, safety, source of supply of vaccine and materials</td>
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<tr>
<td>g. vaccination schedule</td>
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<td>h. Vaccination costs</td>
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<td>i. Strength of recommendation of evidence and/or knowledge sources</td>
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<td>j. Attitudes of health professionals</td>
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The second, related to mass information dissemination campaigns, included social marketing strategies adapted to different subgroups of the population at different times of the year and on a continuous basis. The last category included direct communication techniques with emphasis on those health education actions carried out by medical professionals, nurses and other specialties in the segment in order to address vaccine hesitation and anti-vaccination feelings and activities to promote the importance of immunizations and confidence in vaccines\textsuperscript{30}.

The aforementioned systematic review further identified that all articles included emphasized the importance of understanding the population before implementing any strategy to promote vaccine adherence. The studies analyzed highlighted the importance of understanding the context of anti-vaccination attitudes and, above all, identifying the groups and characteristics of individuals who hesitate to vaccinate their children or even receive vaccine doses on the regular schedule, including identifying their demographic and socioeconomic characteristics, and geographic location. The study’s conclusion states that “signs of vaccine hesitation are unclear, but identifying them quickly is vital to maintain vaccine acceptance” and that “identifying the underlying causes of anti-vaccination and vaccine hesitation, as well as potential targets for these groups and for individuals with anti-vaccination feelings, it is essential to promote that effective strategies can be established to promote vaccine coverage and confidence in vaccines”\textsuperscript{30}.

It remains evident, therefore, that it is not enough to develop any vaccine health education strategy, it is essential, above all, to identify the groups that lack such information, determine the perspective and needs of the target population and adapt intervention approaches to propose interventions capable of alleviating any barriers that prevent the application of vaccines.

In Brazil, however, although vaccine hesitation is a recognized problem, its measurement and recognition is still a challenge\textsuperscript{14,31}. The international literature registers a set of initiatives in this regard, emphasizing the development of instruments capable of recognizing and quantifying vaccine hesitation in different groups and populations. Below, we list some of these instruments: a) The National Network for Immunization Information Survey Instrument\textsuperscript{29}; b) Measuring Confidence in Physicians\textsuperscript{33}; c) Postpartum mothers’ attitudes, knowledge, and confidence regarding vaccination\textsuperscript{34}; d) Immunization Hesitancy Survey\textsuperscript{35}; e) The Vaccine Safety, Attitudes, Training and communication Project\textsuperscript{36}; f) Series of surveys with a strong focus on confidence in the influenza vaccine\textsuperscript{37}; g) Attitudes about Childhood Vaccines Survey\textsuperscript{38}; h) Measuring vaccine hesitancy\textsuperscript{29}.

In Brazil, despite the aforementioned reality, few studies have been developed on the subject and there is no knowledge of standardized strategies capable of identifying individuals with anti-vaccination behaviors and/or feelings. At the national level, a variety of research uses electronic information systems and even documentary research in clinical records, medical records and vaccine cards to show vaccine coverage at state, regional and municipal levels. However, there is no knowledge of any strategy that can effectively and early identify these individuals. Among the main difficulties, the absence of validated instruments that are properly adapted to the national cultural context stands out\textsuperscript{31}.

For all these reasons, it is believed that a valid method to identify individuals hesitant to vaccines, appropriately adapted to the cultural context of Brazil, would allow for better planning of future health interventions within the scope of immunization actions in the Health Unic System (SUS), either by facilitating the identification of parents hesitant to vaccines - and the consequent development of targeted individualized approaches, or for the operationalization of more effective collective actions in the segment of communication in vaccine health.

The development of valid methods to identify individuals hesitant to vaccines is a condition, moreover, for decision makers to recognize the dimension of this problem and, consequently, develop actions aimed at strengthening the NIP and its adherence by parents and by the population in general\textsuperscript{39,40}.

In the wake of this, it is important to mention that an initiative of the Pan American Health Organization and the World Health Organization that, in response to fake news, infodemic and misinformation in the covid-19 pandemic, made recommendations and developed a “kit” of Digital transformation tools to be followed by individuals.
Among the strategies recommended by the institutions are: trusting the WHO; identifying the evidence; avoiding fake news; supporting open science; verifying that the information makes sense, even if it is from a safe source and has already been shared; denouncing harmful rumors; protect privacy; open the data (of quality); if you cannot confirm the source of the information, its usefulness, or if it has been shared before… it is better not to share; confirm whether the information has been shared by others before; participate in social conversations responsibly; share information responsibly; confirm the source, especially in WhatsApp conversations; if the information is not confirmed, do not share; keep learning.41

FINAL CONSIDERATIONS

In order to face the new “Vaccine Rebellion”, it is necessary to put into practice actions that aim to increase confidence in immunization, making it essential to identify individuals and/or groups of hesitant individuals; provide safe and reliable information on this topic; clarify distortions about the vaccination process and about immunizing agents; fight fake news and anti-vaccination activism on the internet; train professionals to act as multipliers of confidence in immunizations; and last but not least, provide society with full guarantee of access to vaccines. Such actions taken together constitute possible ways to face the vaccine hesitancy and the consequent ‘pandemic’ of those unvaccinated.

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